AUDITORY PROCESSING IN INFANTS AT RISK FOR LANGUAGE AND LEARNING IMPAIRMENT AND ASSOCIATION WITH LATER LINGUISTIC DEVELOPMENT

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The research aims to identify early neurocognitive and neuropsychological markers of language and learning disorders (Specific Language Impairment and Developmental Dyslexia), as targets for specific prevention/intervention programs to be applied at very young ages.
Language is a fundamental and complex human attribute and acquisition of this complex system comprises one of the major tasks of infancy.

The acoustic input an infant receive is a continuous deluge of sound information that arrives at the ear in large proportions as brief, rapid, successive bursts with rates in the tens of ms (Choudhury & Benasich, 2001)

The neuropsychological ability to perform fine-grained acoustic analyses is critical to the decoding of the speech stream and the establishment of phonemic maps (Benasich et al., 2002; Kuhl, 2004)
The ability to perform fine-grained acoustic analyses in the tens of milliseconds range is critical to the decoding of the speech stream and the subsequent establishment of phonemic maps.

Rapid Auditory Processing or “RAP”
Most children easily and efficiently acquire language

However, a subset of children have difficult time in acquiring language in the absence of neurological disease, genetic syndromes, mental retardation or hearing loss

**SPECIFIC LANGUAGE IMPAIRMENT:** is characterized by deficits involving phonology, morphosyntax, syntax, semantics, and affects approximately 7% of kindergarten age children (Tomblin et al., 1997).
Specific Language Impairment

Developmental Dyslexia

Behavioral comorbidity between language impairment and developmental dyslexia: Around one third of children with SLI develop dyslexia by elementary school (e.g., McArthur et al. 2000; van Alphen et al., 2004; Catts et al., 2005; Bishop & Snowling, 2004)

Robust genetic correlations have been reported between language and reading traits in general population (ranging .67 to 1.0; Hohnen & Stevenson, 1999) and in affected twins (ranging .53 to .86; Bishop, 2001), supporting the view that dyslexia and SLI share common genes and are not etiologically distinct.
LLI AND AUDITORY PROCESSING

LANGUAGE-BASED LEARNING IMPAIRMENT

PHONOLOGICAL DIFFICULTIES

PHONOLOGICAL DEFICIT HYPOTHESIS (Snowling, 2001)

DEFICITS IN AUDITORY PROCESSING

Evidence for a general deficit in auditory processing (Bretherton & Holmes, 1993; Cantiani et al., 2010; Marshall et al., 2001;)

RESTRICTED TO RAPID AND SHORT SOUNDS

RAPID AUDITORY PROCESSING DEFICIT HYPOTHESIS (Tallal, 1980; Cohen Mimram & Sapir, 2007; Hiervang et al., 2002)
LLI AND RAPID AUDITORY PROCESSING

Interstimulus Interval (ISI) in milliseconds

Percent Correct

Control
Language Impaired

< 40ms - Phonemes
40-350ms - Syllables

Findings show that measures of frequency, rise time, and duration discrimination as well as amplitude modulation (AM) and frequency modulation (FM) detection were most often impaired in individuals (children and adults) with language and learning impairment (Hamalainen et al., 2012)

- Fundamental frequency
- Duration
- Intensity
- Amplitude Modulation (AM) (fluctuations of sound intensity in time)
- Frequency modulation (FM) (fluctuations of sound frequency in time)
Italian children with language impairment (with and without previous history of language impairment) showed difficulties in auditory processing of pairs and sequences of tones and in rhythm discrimination.
OUR STUDY:

Environmental factors

Genetic risk

Early neuropsychological indexes

LANGUAGE LEARNING IMPAIRMENT
OVERALL AIMS:

✓ Establishing the first sample of Italian infants at-risk for language and learning impairment (LLI) to be followed up longitudinally.

✓ Providing extensive data collection of early indexes of cognitive and perceptual functioning, as precursors of LLI, at age 6 months. This information will be enhanced by the investigation of the effects of the environmental and genetic underlying risk factors.

✓ Developing a prognostic model for the emergence of typical and atypical language acquisition.
Examination of dense-array auditory evoked-response brain potentials (dEEG/ERPs) provides non-invasive functional brain measurements of auditory processing skills in infancy.
ERP METHODOLOGY
(Event-Related Potentials recording)
MisMatch Negativity (Response)

Responses    Subtraction wave

Fz

Deviant

MMN

Standard

400 ms

+2 µV

-2 µV

MMR does not require conscious attention to the stimuli and thus provides a measure of fine acoustic discrimination abilities even in preverbal infants.

Oddball Paradigm
PREVIOUS LONGITUDINAL STUDIES

Prof. April A. Benasich - CMBN Rutgers University (U.S.A.)
Infancy Studies Laboratory

LATENCY OF THE N2 COMPONENT

AMPLITUDE OF THE MMR

Choudury & Benasich, 2011 – Clinical Neurophysiology
PREVIOUS LONGITUDINAL STUDIES

Jyväskylä longitudinal study of dyslexia (JLD, Lyytinen et al., 2004)
Dutch Dyslexia Programme (DDP, Van der Leij et al. 2001)

Leppänen et al., 2010

Van Zuijen et al., 2013

Maasssen et al., 2012

Plakas et al., 2012

Hämäläinen et al., 2013

MMR amplitude $R^2 = 0.08-0.20$

MMR topography differentiates fluent and non-fluent at-risk children from controls

MMR amplitude $R^2 = 0.17-.27$

N1-P2 amplitude & N1 latency $R^2 = 0.10-0.14$

MMN amplitude $R^2 = 0.08-0.17$

N250 amplitude $R^2 = 0.07-0.12$

Reading skills

2nd grade

2nd, 3rd, 5th grade

0 m

2 m

1.4 y

1.4-2.4 y

3.4 y

6.5 y
BABYLAB

Standardized scales to assess cognitive, motor and language development

Behavioral tasks and Event-related potentials (ERPs) recoding

Self-administered questionnaires and DNA collection
Research Protocol

- Recruitment during pregnancy
  - Collection of environmental information
    - Familial risk
    - Socio and demographic information
    - Information about pregnancy
  - Familial risk
  - Socio and demographic information
  - Information about pregnancy

- Experimental protocol (6 months)
  - Infant’s assessment:
    - Auditory processing skills
    - Resting states EEG
    - Cognitive, motor and language development (Bayley Scales)

- Collection of DNA sample
- Collection of environmental information
  - Perinatal information

- Parents’ assessment
  - Reading and language tests

- Longitudinal follow-up (12, 20, 24, 36 months)
LANGUAGE AND LEARNING

Early skills

12 months

20 months

24 months

LANGUAGE COMPREHENSION

VOCABULARY DEVELOPMENT:
  • Production
  • Comprehension

COGNITIVE, LINGUISTIC AND BEHAVIORAL DEVELOPMENT
310-word parental-report screening tool for expressive language delay in toddlers, 18-35 months (Rescorla et al., 2014).
EXPERIMENTAL DESIGN

- **Case-control study**: comparison between infants with familial risk for LLI (defined as having certified diagnosis among first-degree relatives of the infant) and control infants

- **Longitudinal design**: Follow up will be performed in order to
  - Confirm/disconfirm the status of risk
  - Develop a prognostic model for the development of language skills

- **Epidemiologic study**: in order to analyze the influence of environmental and genetic variables, and their impact on the intermediate phenotypes.
PARTICIPANTS

Infants enrolled in the project at present time:

N = 118

FH- Group, N = 82  FH+ Group, N = 36

- Specific Language Impairment (N = 14)
- Developmental Dyslexia (N = 17)
- Both Language Impairment and Dyslexia (N = 3)
- Autism Spectrum Disorder (n = 2)

*FH+ means having a first-degree relative affected: a sibling with a clinical diagnosis or a parent scoring above the clinical threshold in both the questionnaire and the standardized testing (reading and non-word repetition).
PARTICIPANTS
linguistic outcome at 20 and 24 months

FH+ Group
N=36

20 months
N = 17
47% < 20 pct

24 months
N = 11
54% < 24 pct
P1/N2: Obligatory responses; obligatorily elicited by the occurrence of stimulus (Ceponiene, Rinne & Näätänen, 2002); associated with auditory detection (P1), sensory memory and feature processing (N2) (Ceponiene, Torki, Alku, Koyama & Townsend, 2008).

Mismatch Response (P3): large positivity peaking at about 300ms from change detection; (Kushnerenko, Ceponiene, Balan, Fellman & Näätänen, 2002), reflect the neural change detection process that occurs when there is any detectable auditory change within a sequence of homogeneous sounds.
1) to test RAP as a risk marker of LLI in 6-month-old Italian infants at-risk versus not-at-risk for LLI, by using age-appropriate techniques that do not require overt responses.

2) to identify developmental pathways from early RAP to later language acquisition, by assessing correlations between RAP and expressive language skills at 20 (and 24) months of age.

Cantiani et al., under review
## PARTICIPANTS

**FH+ (N=24) vs. FH- (N=32)**

Inclusion criteria: 1) both parents native-Italian speakers, 2) gestational age ≥37 weeks, 3) birth-weight ≥2500 grams, 4) APGAR scores at birth at 1’ and 5’ ≥9 and 5) a Bayley Cognitive Score ≥7.

<table>
<thead>
<tr>
<th></th>
<th>FH+ (N = 24)</th>
<th>FH- (N = 32)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (females)</td>
<td>13 (11)</td>
<td>17 (15)</td>
<td></td>
</tr>
<tr>
<td>Birth weight (grams)</td>
<td>3198.5 (325.4)</td>
<td>3265.8 (485.4)</td>
<td>.545</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>39.23 (1.31)</td>
<td>39.61 (1.31)</td>
<td>.295</td>
</tr>
<tr>
<td>Mother’s age (years, months)</td>
<td>34.38 (3.68)</td>
<td>34.53 (4.06)</td>
<td>.883</td>
</tr>
<tr>
<td>Father’s age (years, months)</td>
<td>37.13 (3.69)</td>
<td>37.19 (5.19)</td>
<td>.960</td>
</tr>
<tr>
<td>Mothers’ educational level(^a)</td>
<td>52.92 (16.01)</td>
<td>59.06 (14.45)</td>
<td>.138</td>
</tr>
<tr>
<td>Fathers’ educational level(^a)</td>
<td>40.83 (20.20)</td>
<td>49.38 (17.57)</td>
<td>.097</td>
</tr>
<tr>
<td>Socioeconomic status(^b)</td>
<td>56.04 (22.02)</td>
<td>64.69 (13.73)</td>
<td>.099</td>
</tr>
<tr>
<td>Bayley cognitive subscale</td>
<td>12.48 (1.70)</td>
<td>12.25 (1.81)</td>
<td>.728</td>
</tr>
</tbody>
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at least one first-degree relative 1) had a certified (clinical) diagnosis of LLI and/or 2) performed at least two standard deviations (SD) below the population mean on at least one reading task. n = 7 FH+ for language impairment, n = 14 FH+ for dyslexia and n = 3 for both.

*Cantiani et al., under review*
Mass Univariate Analysis, MMRs, FH- Group (N=32)

Cantiani et al., under review
Mass Univariate Analysis, MMRs, FH- Group (N=32)

Cantiani et al., under review
RESULTS AT 6 MONTHS

FH- (N = 32)

FH+ (N = 24)

Cantiani et al., under review
RESULTS AT 6 MONTHS
Obligatory Components, FH- (N=32) vs FH+ (N=24)

N2* peak latency is delayed in the FH+ group ($M = 328.6, SD = 26.6$) compared to the FH- group ($M = 308.3, SD = 26.1$).

Cantiani et al., under review
RESULTS AT 6 MONTHS
MMRs, FH- (N=32) vs FH+ (N=24)

FH- Group, ch 59

FH+ Group, ch 59

P3 mean amplitude is significantly lower in the FH+ group ($M = 3.77, SD = 2.47$) compare to the FH- group ($M = 5.25, SD = 2.99$)

Cantiani et al., under review
CORRELATIONS WITH THE OUTCOME LANGUAGE SKILLS

LANGUAGE DEVELOPMENT SURVEY (Rescorla et al., 2014)
measure of expressive vocabulary at 20 months (reported by parents)

Cantiani et al., under review
CORRELATIONS WITH THE OUTCOME LANGUAGE SKILLS

LANGUAGE DEVELOPMENT SURVEY (Rescorla et al., 2014)
measure of expressive language at 24 months (reported by parents)

Expressive vocabulary

Mean Length of Utterance (MLU)

Amplitude of the P3
RESULTS OBTAINED BY DIVIDING THE SAMPLE ACCORDING TO THE LINGUISTIC OUTCOME MEASURES

LDS +
N = 16
Words at 20 months
Range 51-227

LDS -
N = 20
Words at 20 months
Range 0-45

Amplitude of the P3
Right
p = .03
RESULTS OBTAINED BY DIVIDING THE SAMPLE ACCORDING TO THE LINGUISTIC OUTCOME MEASURES

\[ p < .01 \]

- **FH-LDS+**
  - n = 11

- **FH-LDS-**
  - n = 10

- **FH+LDS+**
  - n = 5

- **FH+LDS-**
  - n = 10
SUMMARY OF THE RESULTS

- Differences between FH+ and FH- groups emerged for latency of the N2 peak latency and for the amplitude of the P3 (MisMatch Response).

- Correlations revealed a series of statistically significant associations between brain responses at 6 months (latency of P1/N2, amplitude of the N2* and the P3) and expressive vocabulary at 20 and 24 months.

- Brain responses at 6 months differ according to the linguistic outcome (expressive vocabulary at 20 months) irrespectively of the status of risk.

- When considering both status of risk and linguistic outcome, significant differences emerged between FH-LDS+ and FH+LDS- groups.
Brain responses to cross–modal semantic priming in Italian twenty–month–olds

Giulia Melesi, Caterina Piazza, Valentina Riva, Roberta Bettoni, Cecilia Marino, Chiara Cantiani
LINGUISTIC OUTCOME AT 36 MONTHS

- Naming and articulation
- Lexical comprehension
- Syntactic comprehension
  - Simple sentence comprehension
  - Sentences with spatial concepts
- Minimal pair discrimination
  - Place of articulation /cane/ /pane/
  - Manner of articulation – stops /panda/ banda/
  - Manner of articulation – fricatives /cesto/ /gesto/
  - Geminates /note/ /notte/
- Phonological awareness: Syllabic blending
- Morphological manipulation
  - Nominal morphology:
    - Plural (words and non-words)
    - Diminutive
  - Verbal morphology: number subject-verb agreement
- Clitic elicitation: *LO sta pescando – LA sta catturando*
FUTURE DIRECTIONS

SPECIFIC PREVENTION - INTERVENTION PROGRAMS

Early skills

LANGUAGE LEARNING

Behavioral/Cognitive

Plasticity in Developing Brain: Active Auditory Exposure Impacts Prelinguistic Acoustic

Music Enrichment Programs Improve the Neural Encoding of Speech in At-Risk Children
OUR RESEARCH GROUP

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